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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,227	10/03/2003	Hiroaki Ito	053466-0365	8597

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EXAMINER	
MERTZ, PREMA MARIA	

ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/677,227	ITO ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,22-43 and 45-47* is/are pending in the application.

4a) Of the above claim(s) *1-19 and 22-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43 and 45-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/646,188.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/1/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-19, 22-42 were previously withdrawn, and claims 20, 21 and 44 were previously cancelled. Amended claim 43 (7/20/09) and previous claims 45-47 are under consideration by the Examiner.

2. Receipt of applicant's arguments and amendments filed on 7/20/2009 is acknowledged.

3. The following previous rejections and objections are withdrawn in light of applicants amendments filed on 6/14/2007:

(i) the rejection of claims 43, 45-47 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter rejection).

4. Applicant's arguments filed on 7/20/09 have been fully considered and were persuasive in part. The issues remaining and new issues are stated below.

Claim rejections-35 U.S.C. 112, first paragraph, enablement rejection

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claims 43, 45-47, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The deposit of biological material is considered by the Examiner to be necessary for the enablement of the current invention because the claims require availability of the deposit. Elements required for practicing a claimed invention must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. When biological material is required to practice an invention, and if it is not so obtainable or available, the enablement requirements of 35 USC §112, first paragraph, may be satisfied by a deposit of the material. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining human interleukin-6 receptor encoded by the cDNA contained in the plasmid pIBIBSF2R deposited as FERM BP-2232 and it does not appear to be a readily available material. The deposit of FERM BP-2232 in full compliance with 37 CFR §§ 1.803-1.809 would satisfy the requirements of 35 USC §112, first paragraph.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be

irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or Declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-1.809 for additional explanation of these requirements.

Claim rejections-35 USC § 112, first paragraph, scope of enablement

5b. Claims 43, 45-47, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating inflammatory bowel disease by administering an effective amount of monoclonal antibody, PM-1 or MR16-1 against the human IL-6 receptor, does not reasonably provide enablement for a method of treating inflammatory bowel disease by administering "all" interleukin-6 receptor antibodies which bind to human IL-6 receptor encoded by the cDNA contained in the plasmid pIBIBSF2R deposited as FERM BP-2232. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

This rejection is maintained for reasons of record set forth at pages 3-7 of the previous Office action (12/5/2006), page 3 of the previous Office action (8/15/07), pages 2-9 of the previous Office action (1/15/08), pages 2-5 of the previous Office action (7/25/08) and pages 4-5 of the previous Office action (3/12/09).

Applicants argue that claim 43 does not claim a method of "treating all inflammatory diseases," as asserted, but the considerably more defined scope of a "method of treating *inflammatory bowel disease"* (emphasis added) and properly construed, this aspect of the claim is commensurate with the enablement provided by the specification. Applicants also argue that concerning "all" interleukin-6 antibodies, relies on a construction of claim 43 such that it reads not only on antibodies against the IL-6 receptor, *per se,* but also gp130, this issue is respectfully believed to be overcome by the amendment to claim 43, amended claim 43 recites an "anti-interleukin-6 receptor antibody which binds to human interleukin-6 receptor encoded by the

cDNA contained in the plasmid pIBIBSF2R deposited as FERM BP-2232", as described in English-language specification at page 9, lines 30-37, FERM BP-2232 contains DNA which encodes the human IL-6 receptor, and therefore, claims 43 and 45-47 read on antibodies which bind to the IL-6 receptor, *per se*. However, contrary to Applicants arguments, the IL-6 receptor is composed of the IL-6 receptor β subunit (gp130) and the IL-6 receptor α subunit (CD126) and the scope of the claims encompasses antibodies to both subunits of the IL-6 receptor. The instant specification is only enabling for a method of treating inflammatory bowel disease by administering monoclonal antibodies PM-1 or MR16-1 which inhibit the binding of IL-6 to the IL-6 receptor and thereby block the transduction of the biological activity of IL-6 into the cell (see instant specification, page 8, lines 1-24). Monoclonal antibodies PM-1 and MR16-1 are antibodies specific to epitopes on the IL-6 receptor. While the specification discloses that a "IL-6 receptor antibody" (see page 5, lines 9-20) is "preferably" PM-1 (antibody against human IL-6 receptor) or MR16-1 (antibody against mouse IL-6 receptor) and inhibits binding of IL-6 to its receptor and this is the biological property which the administered compound is expected to exhibit, the specification is non-enabling for the unlimited number of compositions encompassed by the scope of the claims and therefore this rejection is maintained for reasons of record.

Claim rejections-35 USC § 112, second paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6a. Claims 43, 45-47, are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is maintained for reasons of record set forth at pages 5-6 of the previous Office action (3/12/09).

Claim 43, last line, is vague and indefinite because it recites "the biological activity of IL-6". There is insufficient antecedent basis for this limitation in the claim.

Applicants argue that the property of "inhibits the biological activity of IL-6" is reasonably ascertainable to those skilled in the art and, hence, is not indefinite, this is especially so when read in the context of the entire claim 43, which recites a method comprising administering an "anti-interleukin-6 receptor antibody" which has the properties of (a) binding to human interleukin-6 receptor encoded by the cDNA contained in the plasmid pIBIBSF2R deposited as FERM BP-2232 (b) blocking signal transduction by IL-6 and (c) inhibiting the biological activity of IL-6, that is, "inhibits the biological activity of IL-6" is one of the several recited properties of the anti-interleukin-6 receptor antibody used in the claimed method. Applicants also argue that the recitation of "inhibits the biological activity of IL-6" is an element that is inherently present when the "anti-interleukin-6 receptor antibody" recited in claim 43 binds to the human interleukin-6 receptor, it is understood that a receptor binds a ligand and, through the process of signal transduction, causes a biological response, and conversely, inhibition of a receptor may, in some cases, inhibit the biological activity of the ligand. Applicants argue that it is therefore understood in view of the specification that "inhibits the biological activity of IL-6" is inherently present in recitation of the specific IL-6 receptor

inhibitor, earlier in claim 43 and it follows that "inhibits the biological activity of IL-6" does have antecedent basis in the claim, such that its recitation is not vague and indefinite. However, contrary to Applicants arguments, Applicants appear to have misconstrued this rejection by the Examiner. The issue here is the limitation "the" biological activity. It is unclear which of the numerous biological activities of IL-6 the administered anti-IL-6 receptor antibody inhibits? This rejection can be obviated by reciting "the" specific biological activity of IL-6 that is inhibited by the administered anti-IL-6 receptor antibody.

Claims 45-47 are rejected as vague and indefinite insofar as they depend on the above rejected claim for their limitations.

Claim rejections-35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7a. Claims 43, 45-47, are rejected under 35 U.S.C. § 102(b) as being anticipated by WO 96/38481.

This rejection is maintained for reasons of record set forth at pages 12-13 of the previous Office action (12/5/2006), pages 4-5 of the previous Office action (8/15/2007), pages 10-11 of the previous Office action (1/15/08), pages 5-6 of the previous Office action (7/25/08) and pages 6-7 of the previous Office action (3/12/09).

Applicants argue that at items 7 and 7a, pages 6-7, it is asserted that claims 43 and 45-47 are anticipated by WO 96/38481, which allegedly discloses antibodies which bind to, and inhibit, gp 130, solely to advance prosecution, pending claim 43 reads on antibodies against IL-6 receptor, *per se,* WO 96/38481 does not disclose a method of treating inflammatory bowel disease comprising administering to a subject in need thereof an anti-interleukin-6 receptor antibody which binds to human interleukin-6 receptor encoded by the cDNA contained in the plasmid pIBIBSF2R deposited as FERM BP-2232, blocks signal transduction by IL-6 and inhibits the biological activity of IL-6 and therefore WO 96/38481 does not anticipate claims 43 and 45-47. However, contrary to Applicants arguments, the IL-6 receptor is composed of the IL-6 receptor β subunit (gp130) and the IL-6 receptor α subunit (CD126). In the absence of disclosure of whether the human interleukin-6 receptor encoded by the cDNA contained in the plasmid pIBIBSF2R deposited as FERM BP-2232 is the IL-6 receptor β subunit (gp130) or the IL-6 receptor α subunit (CD126), the method disclosed in the reference anticipates claims 43, 45-47 because gp130 is the signal transducing subunit of the IL-6 receptor. Therefore this rejection is maintained for reasons of record.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at

the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8a. Claims 43-47 are rejected under 35 U.S.C. § 103 as being unpatentable over WO 96/38481 in view of Queen et al. (U.S. Pat No. 5,530,101).

This rejection is maintained for reasons of record set forth at pages 13-14 of the previous Office action (12/5/2006), pages 5-6 of the previous Office action (8/15/2007) and pages 12-13 of the previous Office action (1/15/08), pages 7-9 of the previous Office action (7/25/08), and pages 7-8 of the previous Office action (3/12/09).

Applicants argue that neither reference, or their combination, discloses or even suggests a method of treating inflammatory bowel disease comprising administering to a subject in need

thereof an anti-interleukin-6 receptor antibody which binds to human interleukin-6 receptor encoded by the cDNA contained in the plasmid pIBIBSF2R deposited as FERM BP-2232, blocks signal transduction by IL-6 and inhibits the biological activity of IL-6. However, contrary to Applicants arguments, the additional limitation (in the claimed method) that the administered anti-interleukin-6 receptor antibody binds to human interleukin-6 receptor encoded by the cDNA contained in the plasmid pIBIBSF2R deposited as FERM BP-2232 and blocks signal transduction by IL-6 encompasses an antibody to gp130 because gp130 is the signal transducing subunit of the IL-6 receptor. It is unclear from the claim whether the recited cDNA encodes the IL-6 receptor α subunit (CD126) or gp130. Since the WO 96/38481 reference teaches targeting gp130 with monoclonal antibodies to treat inflammatory bowel disease, and Queen teaches the production of humanized antibodies, the claimed references render obvious the claimed invention and this rejection is maintained for reasons of record.

Conclusion

No claim is allowed.

Claims 43, and 45-47, are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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